IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	**Group Art Unit:** 1644
HENRY LAMPARSKI et al.	**Examiner:** Marianne-DiBrino
Serial No.: 09/780,748	
Filed: February 9, 2001	
For: **METHOD FOR PREPARING MEMBRANE VESICLES**	

RESPONSE TO RESTRICTION REQUIREMENT

MAIL STOP PATENT APPLICATION
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In response to the Office Action Summary mailed on January 12, 2006, the Applicants elect Group I, claims 6-9, 11-23, 35 and 36 drawn to a method of preparing an immunogenic membrane vesicle, and pharmaceutical composition thereof, comprising contacting the vesicle with the disclosed species of a class-I restricted peptide, and under conditions allowing the peptide to bind an antigen-presenting molecule a the surface of the membrane vesicle and to the method of preparing a pharmaceutical product comprising an immunogenic membrane vesicle. Applicants have also added new claims 37-43 which also define a single inventive concept with the elected claims.

CERTIFICATE OF ELECTRONIC FILING

I hereby certify that I have reasonable basis to expect that that this paper or fee (along with any referred to as being attached or enclosed) was transmitted electronically to Mail Stop Patent Application, Commissioner For Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: April 11, 2006

Karen Johnson

IN THE CLAIMS:

1.- 5. (Cancelled)

6. (Original) The method of claim 1, wherein the peptide is a class-I restricted peptide.

7. (Original) The method of claim 1, wherein the peptide is a class-II restricted peptide.

8. (Original) The method of claim 1, wherein the vesicles are contacted with a mixture of peptides.

9. (Original) The method of claim 8 wherein the vesicles are contacted with a peptide eluate of tumor cells.

10. (Cancelled)

11. (Original) The method of claim 1 wherein the immunogenic membrane vesicle comprises a complex of an exogenous class-I peptide bound to an HLA class I molecule, further comprising (i) subjecting an isolated or purified membrane vesicle to a selected acid medium, (ii) contacting the membrane vesicle with a class I-restricted peptide in the presence of beta2-microglobulin, under conditions allowing the peptide to complex with an HLA class I molecule at the surface of the membrane vesicle, and (iii) collecting the membrane vesicle.

12. (Original) The method of claim 11, wherein step (i) comprises subjecting the membrane vesicles to a medium at a pH comprised between about 3 and about 5.5 for less than 15 minutes.

13. (Original) The method of claim 11, wherein step (ii) comprises contacting the membrane vesicle with 0.005 to 50 μg/ml of class I-restricted peptide in the presence of beta2-microglobulin.

14. (Original) The method of claim 1 wherein the immunogenic membrane vesicle comprises a complex of an exogenous class-I peptide bound to an HLA class I molecule, further comprising (i) contacting the membrane vesicle with a class I-restricted peptide in the absence of beta2-microglobulin, (ii) subjecting the membrane vesicle to a selected acid medium under conditions allowing the peptide to exchange with any endogenous peptide for binding with an HLA class I molecule at the surface of the membrane vesicle, (iii) neutralizing the medium to stop the exchange and stabilize the complex formed in (ii) and, (iv) collecting the membrane vesicle.

15. (Original) The method of claim 14, wherein step (ii) comprises subjecting the membrane vesicle to a selected acid medium at a pH comprised between about 4 and about 5.5. for less than 2 hours.

16. (Original) The method of claim 14, wherein step (i) comprises contacting the membrane vesicle with 5 to 500 μg/ml of class I-restricted peptide in the absence of beta2-microglobulin.

17. (Original) The method of claim 11, wherein the peptide is selected from the group consisting of a tumor antigen, a viral antigen, a parasite antigen and a bacterial antigen.

18. (Original) The method of claim 14, wherein the peptide is selected from the group consisting of a tumor antigen, a viral antigen, a parasite antigen and a bacterial antigen.

19. (Original) A method of preparing peptide-loaded membrane vesicles, comprising :

a) culturing of a population of antigen-presenting cells under conditions allowing the release of membrane vesicles by antigen-presenting cells,

b) purifying or enriching the membrane vesicles, and

c) contacting the membrane vesicles with a peptide under conditions allowing the peptide to bind an MHC molecule at the surface of the membrane vesicles to produce peptide-loaded membrane vesicles.

20. (Original) The method of claim 19 wherein the cultured population antigen-presenting cells are dendritic cells.

21. (Original) The method of claim 19, wherein the membrane vesicles are subjected to a selected acid medium.

22. (Original) A method of preparing peptide-loaded membrane vesicles, comprising:

a) obtaining a population of immature dendritic cells

b) culturing the population of immature dendritic cells under conditions allowing the release of membrane vesicles by immature dendritic cells,

c) purifying or enriching the membrane vesicles, and

d) contacting the membrane vesicles with a peptide under conditions allowing the peptide to bind an MHC molecule at the surface of said membrane vesicles to produce peptide-loaded membrane vesicles.

23. (Original) The method of claim 22, wherein the membrane vesicles are subjected to a selected acid medium.

24. – 34. (Cancelled)

35. (Original) A method of preparing a pharmaceutical product comprising an immunogenic membrane vesicle and a pharmaceutically acceptable diluent or carrier comprising (i) isolating a membrane vesicle from a biological sample, (ii) loading the isolated membrane vesicle with an immunogenic peptide or lipid to produce an immunogenic membrane vesicle, and (iii) contacting the immunogenic membrane vesicle with a pharmaceutically acceptable diluent or carrier.

36. (Original) The method of claim 35 further comprising the step of removing unbound immunogenic peptide or lipid.

37. (New) A method of characterizing membrane vesicles obtained by a method according to claim 6 or 7, comprising contacting the membrane vesicles in parallel with two or more antibodies specific for markers of membrane vesicles and determining the formation of antigen-antibody immune complexes.

38. (New) The method of claim 37, wherein the membrane vesicles are loaded onto solid supports, such as beads.

39. (New) The method of claim 37, wherein the two or more antibodies are selected from the group consisting of anti CD11c, anti CD11b, anti HLA abc, anti CD81, anti CD63, anti CD58, anti CD1a, anti CD1b, anti CD9, anti CD86, anti CD82, anti CD83, and anti lactadherin and combinations thereof.

40. (New) A method of characterizing the activity of a preparation of membrane vesicles obtained by a method according to claim 6 or 7, comprising contacting super-antigen-loaded membrane vesicles with T cells in the presence of accessory cells, and determining the activation of the T cells.

41. (New) The method of claim 40, wherein the membrane vesicles are loaded with super-antigen.

42. (New) The method of claim 40, wherein the membrane vesicles are produced form producing cells loaded with super-antigen.

43. (New) A method of dosing membrane vesicles in a sample, comprising: loading the sample onto a solid support, contacting the support with an anti-class I antibody and determining the presence of antibody-antigen immune complexes.

REMARKS

Applicants respectfully traverse the restriction to claim grouping I – VI. Applicants maintain that the different claims, corresponding to the various elected groups, may be patentably distinct. However, Applicants submits that groups I and II should not be subject to restriction because the base claims recites the option of a peptide or a lipid and the common principle of "conditions allowing the peptide or lipid to bind an antigen-presenting molecule at the surface of the membrane vesicle" unifies the two principles such that the Examiner's search should yield the pertinent art to the claims in the two groups and that examination of the claim as written would not be unduly burdensome.

The same rationale applies with respect to the restriction between groups III and IV drawn to pharmaceutical compositions comprising an immunogenic membrane vesicle loaded with an immunogenic lipid or peptide. Applicants also note that the requirement for the presence of an immunogenic membrane vesicle unifies both the prior art search and the pertinent points of the examination for those claimed groups.

Applicant also submit that given the recitation of the structural limitations defining how the "immunogenic membrane vesicle" was obtained in claims 29-30, that the option to restrict examination under MPEP 806.05(f) should be avoided. Applicants note that the option for restriction under 806.05(f) is permissive and that the plain language of the claims indicates that the process and product are not materially different.

The Commissioner is also authorized to charge any fees required by the filing of this papers, and to credit any overpayment to Orrick Herrington & Sutcliffe's Deposit Account No. **150665.**

Respectfully submitted,

ORRICK, HERRINGTON & SUTCLIFFE LLP

Dated: April 11, 2006

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